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| EXAMINER |
|---|
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| ART UNIT | PAPER NUMBER |
|---|---|
| 1647 | 13 |

DATE MAILED: 02/11/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/704,272 | ATTIE ET AL. | |
| | Examiner | Art Unit | |
| | Sandra Wegert | 1647 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *15 November 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *4,7-10 and 12-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5,6 and 11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☒ The proposed drawing correction filed on *13 May 2002* is: a)☒ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5,6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

***Status of Application, Amendments, and/or Claims***

The Information Disclosure Statement, received 6/11/01, has been entered into the record as Paper 5. The Supplemental Information Disclosure Statement, received 8/6/01(Paper 6) has been entered. Applicant's election of Invention I, (claims 1, 2, 3, 5, 6 and 11) in Paper No. 12 is acknowledged. Applicant elected Invention I with traverse. The traversal is on the ground(s) that, as far as Inventions I-IV are concerned, they are interlinked as far as subject matter and that a search for any one of the Inventions would encompass the material relevant to any other Invention. Applicant's traversal also implied that it is in the best interests of the Patent Office not to use restriction requirements that are so prolific. Applicant's arguments are not persuasive, however, since Inventive Groups I-IV in question were properly restricted as the methods are practiced with materially different process steps for materially different purposes and each method requires a non-coextensive search because of different starting materials, process steps, goals and measured endpoints. The methods of groups I-IV each require different research or clinical personnel, different techniques and materials, different patient populations, and are done for different purposes and with different measured endpoints. In addition, since a complete search of the art includes a search of the art that renders an invention obvious as well as anticipatory, the additional searches required for examination of Inventions I-IV would be extensive, thus presenting an undue burden for the examiner. In addition, to address the Applicant's argument which suggested that it is in the best interests of the Patent Office to examine fewer Inventions, it should be kept in mind that the restriction was in compliance with

current USPTO guidelines (see MPEP 802.01). Each Patent Application is prosecuted only on its merits and only according to applicable Patent laws and regulations.

It should be noted that claims will be examined insofar as they read on the elected Invention. Claims 4, 7-10 and 12-21 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected Inventions, there being no allowable generic or linking claim.

Claims 1-3, 5, 6, 11 are under examination in the Instant Application.

## ***Informalities***

### *Specification*

The disclosure is objected to because of the following informalities:

***URL's***

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (for example, p. 20, line 11). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

## **Claim Objections/Rejections**

**35 *USC § 112, first paragraph - lack of enablement***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

**The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.**

Claims 1-3, 5, 6 and 11 are rejected under 35 U.S.C. 112, first paragraph, because the subject matter was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The specification is not enabling for the limitations of the claims wherein cholesterol uptake in the gut is inhibited by administering an ABC1 transporter inhibitor.

Claims 1-3, 5, 6 and 11 read on a method of inhibiting cholesterol transport across the lumen of the gut of a human or animal, by administering an inhibitor of ABC1. Dependent claims recite sulfonylurea compounds as ABC inhibitors and agents given orally.

The specification discloses the *WHAM* mutation in chickens, in which a single nucleotide substitution results in an amino acid change at residue 89 of an ABC transporter. The specification documents the phenotypes of WHAM chickens as to pigmentation, phospholipid disposition and cholesterol transport (Specification pp. 25-27). *WHAM* chickens appear to share similarities to humans with Tangier's disease, namely: retention of cholesterol esters in skin and connective tissues (Lawn, et al, 1999, J. Clinical Investigation, 104: R25). Similarly, mutations in other human ABC transporters (ABCG5 and ABCG8) result in the hyperaccumulation of dietary plant sterols and cholesterol (Berge, et al, 2000, Science, 290: 1771) in homozygous individuals.

The instant Specification documents the *WHAM* mutation in chickens and uses the sulfonylurea *glyburide* to inhibit cholesterol transport in normal mouse macrophages. However,

the claims read on a method of inhibiting cholesterol uptake in the gut of an individual or animal, and there is no enabling discussion or working examples disclosed in the instant application as to how to practice the method of inhibiting cholesterol uptake from the lumen of the gut *in-vivo*. Since regulation of cholesterol transport from the diet is complex, and involves more receptors than ABC receptors, and more ABC receptors than ABC1 (Berge, et al, 2000, Science, 290: 1771; Lawn, et al, 1999, J. Clinical Investigation, 104: R25) and possibly different mechanisms of cholesterol transport control in normal individuals, the effects of administering an ABC1 antagonist to inhibit cholesterol transport *in-vivo* are unpredictable.

In In re Wands, 8USPQ2d, 1400 (CAFC 1988) page 1404, the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Due to the large quantity of experimentation required to determine how to administer, control side effects, and use an ABC inhibitor to inhibit cholesterol transport across the gut, the lack of direction or guidance in the specification regarding the same, the lack of working examples that use a sulfonylurea *in-vivo*, the state of the art showing the complexities of cholesterol transport regulation, and the breadth of the claims which embrace in-vivo inhibition of cholesterol transport even in normal individuals, --undue experimentation would be required of the skilled artisan to make and use the claimed invention in its full scope.

***35 USC § 112, first paragraph – written description.***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> **The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.**

Claims 1-3, 5, 6 and 11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

Claims 1-3, 5, 6 and 11 read on a method of inhibiting cholesterol transport across the lumen of the gut of a human or animal, by administering an inhibitor of ABC1. Dependent claims recite sulfonylurea compounds as ABC inhibitors and agents given orally.

The specification teaches use of glyburide to inhibit ABC1 activity in macrophages. However, the specification does not teach functional or structural characteristics of the claimed ABC1 inhibitors. The description of one sulfonylurea compound (glyburide) is not adequate written description of an entire genus of functionally equivalent ABC1 inhibitors. In addition, the use of glyburide does not provide sufficient written-description for the use of all sulfonylurea compounds.

*Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*" (See page 1117). The specification does not "clearly allow persons of

ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116).

With the exception of the single compound referred to above, the skilled artisan cannot envision the detailed chemical structure of the encompassed ABC1 inhibitor, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the methods disclosed. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of using it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only use of glyburide, but not the full breadth of the claims meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

**Claim Rejections - 35 USC § 112, second paragraph-indefiniteness.**

The following is a quotation of the second paragraph of 35 U.S.C. 112:

**The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.**

Claim 5 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 5 states that the agent acts by "inhibiting the activity" of the ABC1 protein. It is not clear from the claim or from the Specification what is meant by this term; similarly, it is not clear how the claimed subject matter from Claim 5 is differentiated from Claim 3, from which the claim depends.

***Conclusion***

No claims are allowed.

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

***Advisory Information***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Wegert whose telephone number is (703) 308-9346. The examiner can normally be reached Monday - Friday from 8:30 AM to 5:00 PM (Eastern Time). If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached at (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

SLW
2/4/03

Gary L Kunz
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